Remarks

Claims 1-17, 20-24 and 26-29 are amended herein. Claims 18, 19, and 30-56 are canceled herein, without prejudice to renewal. New claims 60-77 are added herein.

Support for the amendment of claims 1, 5, 12, and 26 can be found in the specification at page 10, line 20 through page 11, line 4. Support for the amendment of claims 2-4, 7, 8, 28, and 29 can be found in the specification at page 11, lines 5-17. Claims 2-4, 7, 8, 28, and 29 are also amended to correct form. Support for the amendment to claims 9-11 can be found in the specification at page 3, line 36 through page 4, line 2 and at page 39, line 7 through page 40, line 5. Claims 10 and 11 are also amended to correct dependency. Claims 6, 9-11, 13-24, and 27 are amended to correct form. Claim 16 is also amended to correct a typographical error. Support for new claims 60, 61, 65-67, and 71-73 can be found in the specification at page 11, lines 5-17. Support for new claims 62-64, 68-70, and 74-76 can be found in the specification at page 10, line 20 through page 11, line 4. Support for new claim 77 can be found in the specification at page 39, lines 18-19 and in original claim 12.

No new matter is added. Examination of the subject application is respectfully requested.

Restriction Requirement

Applicants elect with traverse Examiner's Group I (claims 1-30, and 57), drawn to a method of inhibiting endothelial cell growth and angiogenesis using calreticulin protein. Applicants submit that the subject matter of Group V (claims 58 and 59), drawn to a method of inhibiting radiation and chemotherapy induced injury, should be classified in the same group as the claims in Group I. Applicants submit that it is not an undue burden on the Examiner to include the subject matter of claims 58 and 59 with the subject matter of the claims in Group I. Reconsideration of the restriction requirement is respectfully requested.

Conclusion

If any minor matters remain to be addressed prior to examination, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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Marked-up Version of Amended Claims
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)

In the claims:

1. (Once amended) A method of inhibiting endothelial cell growth, comprising:

contacting an endothelial cell[s] with a polypeptide comprising an amino acid sequence at least 90% homologous to an amino acid sequence as set forth in SEQ ID NO: 2, or a therapeutically effective fragment thereof,

thereby inhibiting endothelial cell growth [pharmaceutical composition comprising at least one protein selected from the group consisting of:

(a) therapeutically effective fragments of calreticulin;

(b) therapeutically effective variants of calreticulin; and

(c) calreticulin].

2. (Once amended) The method of claim 1, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 6 [pharmaceutical composition further comprises a pharmaceutically acceptable carrier].

3. (Once amended) The method of claim 1, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 8 [of calreticulin comprises a polypeptide of about 180 amino acids from the N-terminus of calreticulin].

4. (Once amended) The method of claim 1, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 5 [of calreticulin consists essentially of an amino acid sequence selected from the group consisting of:

(a) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 3;

(b) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 4;

(c) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 5;

(d) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 6;

(e) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 8; and

f) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 9].

5. (Once amended) A method of inhibiting angiogenesis in a subject, comprising:

administering to the subject a composition comprising a polypeptide comprising an amino acid sequence at least 90% homologous to an amino acid sequence as set forth in SEQ ID NO: 2, or a therapeutically effective fragment thereof,

thereby inhibiting angiogenesis in the subject [an effective amount of a pharmaceutical composition comprising at least one protein selected from the group consisting of:

(a) therapeutically effective fragments of calreticulin;

(b) therapeutically effective variants of calreticulin; and

(c) calreticulin].

6. (Once amended) The method of claim 5_2 wherein the [pharmaceutical] composition further comprises a pharmaceutically acceptable carrier.

7. (Once amended) The method of claim 5_2 wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 6 [of calreticulin comprises a polypeptide of about 180 amino acids from the N-terminus of calreticulin].

8. (Once amended) The method of claim 5_2 wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 8 [of calreticulin consists essentially of an amino acid sequence selected from the group consisting of:

(a) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 3;

(b) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 4;

(c) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 5;

(d) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 6;

(e) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 8; and

f) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 9].

9. (Once amended) The method of claim 5, wherein the angiogenesis is associated with a disease, other than a tumor, [that is] and wherein the disease is associated with neovascularization.

10. (Once amended) The method of claim [9]5, wherein [angiogenesis is inhibited in] the subject has a disease associated with angiogenesis or neovascularization [selected from a group consisting of] comprising diabetic retinopathy, retrolental fibroplasia, trachoma, neovascular glaucoma, psoriasis, angiofibromas, immune-inflammation, atherosclerosis, excessive wound repair, retinal neovascularization, macular degeneration, corneal graft rejection, contact lens overwear, Crohn's disease [and] or non-immune inflammation.

11. (Once amended) The method of claim [9]5, wherein the subject has a disease [is selected from a group consisting of] associated with angiogenesis or neovascularization comprising rheumatoid arthritis, systemic lupus erythematosus, thyroiditis, Goodpasture's Syndrome, systemic vasculitis, scleroderma, Sjogren's syndrome, sarcoidosis [and] or primary biliary cirrhosis.

12. (Once amended) A method of treatment of Kaposi's sarcoma in a subject, comprising:

administering to the subject an effective amount of [pharmaceutical] a composition comprising a polypeptide comprising an amino acid sequence at least 90% homologous to an amino acid sequence as set forth in SEQ ID NO: 2, or a therapeutically effective fragment thereof,

thereby treating Kaposi's sarcoma in the subject [at least one protein selected from the group consisting of:

(a) therapeutically effective fragments of calreticulin;

(b) therapeutically effective variants of calreticulin; and

(c) calreticulin; and

(d) therapeutically effective variants of the fragments of (a)].

13. (Once amended) The method of claim 5_2 further comprising [providing a second] administering an anti-angiogenic agent [selected from a group consisting of] comprising platelet-factor-4, IP-10 (interferon (IFN)-γ inducible protein-10), MIG (Monokine induced by IFN-γ), INF-γ, IFN-α, angiostatin, endostatin, fumagillin, AGM-1470, thrombospondin, a fragment of prolactin, antibody against the integrin $\alpha_v\beta_3$, IL-12, cleaved conformation of the serpin antithrombin, thalidomide, [and] or a mixture[s] thereof.

14. (Once amended) The method of claim 5_2 further comprising administering a chemotherapeutic agent.

15. (Once amended) The method of claim 5_2 further comprising administering a hormone.

16. (Once amended) The method of claim 5_2 further comprising administering an anti-[inflamatory] inflammatory agent.

17. (Once amended) The method of claim 5_2 further comprising administering an anti-viral agent.

Please cancel claims 18 and 19 without prejudice to renewal.

20. (Once amended) The method of claim 5, wherein the subject [angiogenesis is inhibited in] has periodontal disease.

21. (Once amended) The method of claim 20, further comprising administering an antibiotic.

22. (Once amended) The method of claim 5, wherein the subject has a [angiogenesis is inhibited in] radiation induced injury.

23. (Once amended) The method of claim 5, wherein the subject has a [angiogenesis is inhibited in] chemotherapy induced injury.

24. (Once amended) The method of claim 5, wherein the [pharmaceutical] composition inhibits angiogenesis, [which] wherein angiogenesis is stimulated in the subject by an angiogenesis inducer [selected from a group consisting of,] comprising basic fibroblast growth factor, acidic fibroblast growth factor, Vascular Endothelial Growth Factor (VEGF), hepatocyte growth factor, Interleukin (IL)-15, IL-8, platelet-derived endothelial cell growth factor (PDECGF), Transforming Growth Factor (TGF)-β, Tumor necrosis Factor (TNF)α, angiogenin, cripto, [and] or a mixture[s] thereof.

25. (Reiterated) The method of claim 5, wherein the subject is immunocompromized due to T-lymphocyte deficiency.

26. (Once amended) A method of inhibiting tumor growth in a subject, comprising:

contacting tumor cells with an effective amount of a [pharmaceutical] composition comprising a polypeptide comprising an amino acid sequence at least 90% homologous to an amino acid sequence as set forth in SEQ ID NO: 2, or a therapeutically effective fragment thereof,

thereby inhibiting tumor growth in the subject [at least one protein selected from the group consisting of:

(a) therapeutically effective fragments of calreticulin; and

(b) therapeutically effective variants of calreticulin].

27. (Once amended) The method of claim 26, wherein the [pharmaceutical] composition further comprises a pharmaceutically acceptable carrier.

28. (Once amended) The method of claim 26, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 6 [of calreticulin comprises a polypeptide of about 180 amino acids from the N-terminus of calreticulin].

29. (Once amended) The method of claim 26, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 8 [of calreticulin consists essentially of an amino acid sequence selected from the group consisting of:

(a) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 3;

(b) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 4;

(c) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 5;

(d) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 6;

(e) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 8; and

f) at least 5 contiguous amino acid residues of the sequence shown in Seq. I.D. No. 9].

Please cancel claims 30-56 without prejudice to renewal.

57. (Once amended) The method of claim 1, wherein the therapeutically effective fragment of calreticulin consists essentially of [an amino acid sequence selected from the group consisting of] :

(a) [the] an amino acid sequence as set forth in [shown in] SEQ ID NO: 5;

(b) [the] an amino acid sequence as set forth in [shown in] SEQ ID NO: 6;

(c) [the] an amino acid sequence as set forth in [shown in] SEQ ID NO: 8;

(d) [the] an amino acid sequence as set forth in [shown in] SEQ ID NO: 9; [and] or

(e) an amino acid sequence as set forth in SEQ ID NO: 4 [amino acid sequences comprising fragments and variants of the sequences of (a), (b), (c), and (d), wherein the amino acid sequence inhibits tumor growth].

58. (Reiterated) A method of inhibiting radiation induced injury, comprising contacting cells with a pharmaceutical composition comprising at least one protein selected from the group consisting of:

(a) therapeutically effective fragments of calreticulin;

(b) therapeutically effective variants of calreticulin; and

(c) calreticulin.

59. (Reiterated) A method of inhibiting chemotherapy induced injury, comprising contacting cells with a pharmaceutical composition comprising at least one protein selected from the group consisting of:

(a) therapeutically effective fragments of calreticulin;

(b) therapeutically effective variants of calreticulin; and

(c) calreticulin.

Please add the following new claims:

--60. (New) The method of claim 1, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 4.

61. (New) The method of claim 1, wherein the therapeutically effective fragment comprises SEQ ID NO: 9.

62. (New) The method of claim 1, wherein the polypeptide comprises an amino acid sequence at least 95% homologous to an amino acid sequence as set forth in SEQ ID NO: 2.

63. (New) The method of claim 62, wherein the polypeptide comprises an amino acid sequence at least 98% homologous to an amino acid sequence as set forth in SEQ ID NO: 2.

64. (New) The method of claim 63, wherein the polypeptide comprises an amino acid sequence as set forth in SEQ ID NO: 2.

65. (New) The method of claim 5, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 5.

66. (New) The method of claim 5, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 4.

67. (New) The method of claim 5, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 9.

68. (New) The method of claim 5, wherein the polypeptide comprises an amino acid sequence at least 95% homologous to an amino acid sequence as set forth in SEQ ID NO: 2.

69. (New) The method of claim 68, wherein the polypeptide comprises an amino acid sequence at least 98% homologous to an amino acid sequence as set forth in SEQ ID NO: 2.

70. (New) The method of claim 69, wherein the polypeptide comprises an amino acid sequence as set forth in SEQ ID NO: 2.

71. (New) The method of claim 26, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 5.

72. (New) The method of claim 26, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 4.

73. (New) The method of claim 26, wherein the therapeutically effective fragment comprises an amino acid sequence as set forth in SEQ ID NO: 9.

74. (New) The method of claim 26, wherein the polypeptide comprises an amino acid sequence at least 95% homologous to an amino acid sequence as set forth in SEQ ID NO: 2.

75. (New) The method of claim 74, wherein the polypeptide comprises an amino acid sequence at least 98% homologous to an amino acid sequence as set forth in SEQ ID NO: 2.

76. (New) The method of claim 75, wherein the polypeptide comprises an amino acid sequence as set forth in SEQ ID NO: 2.

77. (New) The method of claim 5, wherein the subject has Kaposi sarcoma.--